European Scientific Journal February 2014 /SPECIAL/ edition vol.3 ISSN: 1857 – 7881 (Print) e - ISSN 1857- 7431

AMINOLYSIS OF Z-4-FURYLIDENE OXAZOLIN-5-ONE DERIVATIVES-CONFIGURATION AND KINETICS

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Abstract

The kinetics of ring opening of (Z)-4-(substitutedarylidene)-2-aryloxazolin-5-ones 1_{a-e} with piperidine in acetonirile has been investigated in the temperature range (25-50^0C) which were found to be a second-order reaction, the estimated positive ρ values, thermodynamic parameters and reaction rate constants are consisting with the suggested a stepwise mechanism, where the first stage is a slow perpendicular nucleophilic attack of piperidine on carbonyl group forming the intermediate ($T^{\#}$) passing through a cyclic zwitterionic transition state followed by expelling of the leaving group. As well as the products of the reaction $\underline{3}_{a-e}$ will be identified and determined their configuration assignments which based on NMR analysis, applying the ^{1}H-NMR additivy increment rules and the gated decoupling technique ^{13}C-NMR ($^3J_{CH}$) which indicates that the compounds 3_{a-e}, exclusively have the Z-configuration.

Keywords: Oxazolinones, azomethine carbon, piperdine

Introduction

Oxazolinones are very important starting materials in synthesis of large organic compounds which posses a wide spectrum of biological activities[1-5].The substituted oxazolin-5-one (1) derivatives were prepared by Plochl-Erlenmeyer or microwave irradiation conditions.[6-10]

The reaction of oxazolinone with amino compounds gave various types of amides[11-15].

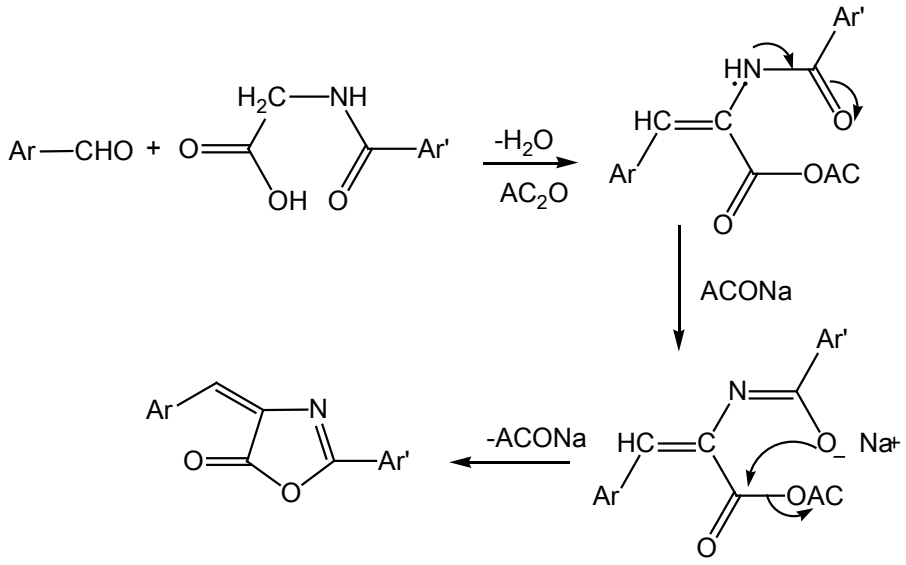
In previous work[11-12] the reaction of oxazolinones with cyclohexylamine, β-aminoethanol, isopropyl amine and benzyl amine underwent ring opening to give the corresponding amides, while the latter amine in the presence of anhydrous zinc chloride gave the corresponding imidazolinones[16]. Similarly the reaction of oxazolinones with 2-aminothiophenol in acidic medium gave the corresponding benzothiazols[17], while in dioxane the lactone underwent ring cleavage to form the corresponding benzamides. Hydrazinolysis of oxazolinones with substituted phenyl hydrazines gave the corresponding hydrazides of α,β-disubstituted acrylic acid[18], imidazoline, triazine[19] and phthalazine[20] derivatives.

Condensation of the unsaturated oxazolinones with urea and thiourea gave the corresponding imidazol-5-ones[21]. El-Nagdy et.al[22] reported that the reaction of substituted oxazolin-5-ones with aniline derivatives afforded the corresponding benzoxazin-4(H)-one and quinazoline derivatives while in the presence of anhydrous zinc chloride the corresponding imidazolinones were obtained[23-28]. These compounds exhibited mild anti-convulsant activity in the pentatetrazole test. On the other hand, 2-aryl-H-pyrimidines have been synthesized by the condensation of 1,8-diaminonaphthalenes with oxazolin ones, followed by pyrolysis[29]. Imidazolin-5-one derivatives were synthesized by condensation of oxazolinones with perimidine derivatives, 2-aminothiophenol and 2-aminothiazole which showed bactericidal and fungicidal activity[30-33].

This work was planned as our interest in the reactions of oxazolinones with different nucleophile. The nucleophile chosen for this study is piperidine in acetonitrile, while the oxazolinone contains a new aromatic moiety (furyl ring). The products of the reaction of oxazolinones with piperidine will be identified and determined their configuration assignments which based on NMR analysis, applying the ^{1}H-NMR additivy increment rules and the gated decoupling technique ^{13}C-NMR ($^{3}J_{CH}$) in order to elucidate the mechanism of this important kind of organic reactions. Furthermore the study investigates the effect of substituents having different electronic character in the non-leaving and leaving groups of oxazolinones. The titled reactions will be measured kinetically in acetonitrile solvent, as well as plausible mechanisms will be suggested.

Results and Discussion

The condensation of aromatic aldehydes e.g. 5-substituted furfural with substituted hippuric acid and acetic anhydride in the presence of catalytic amount of sodium acetate afforded the formation 4-furylidene-2-phenyloxazolin-5-ones[1-4] $\underline{1}_{a-e}$ Scheme (1).

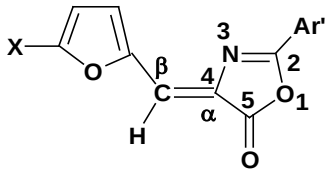


$\underline{1}_a$, Ar = furyl, Ar' = C_6H_5 ; $\underline{1}_b$, Ar = 5-CH_3furyl, Ar' = C_6H_5 ;

$\underline{1}_c$, Ar = 5-Clfuryl, Ar' = C_6H_5 ; $\underline{1}_d$, Ar = furyl, Ar' = 4-$CH_3C_6H_4$;

$\underline{1}_e$, Ar = furyl, Ar' =4-ClC_6H_4.

The furylidene moiety may have either E- or Z- orientation about the exocyclic double bond. Earlier publication reported the presence of E-isomer[34-37]. However, The UV absorption[38-40] resonance, Rahman[41], NMR[42] and X-ray studies[43] indicated that the Z-isomer was thermodynamically stable. However the Z-isomer can be converted into E-isomer by treatment with HBr[44].

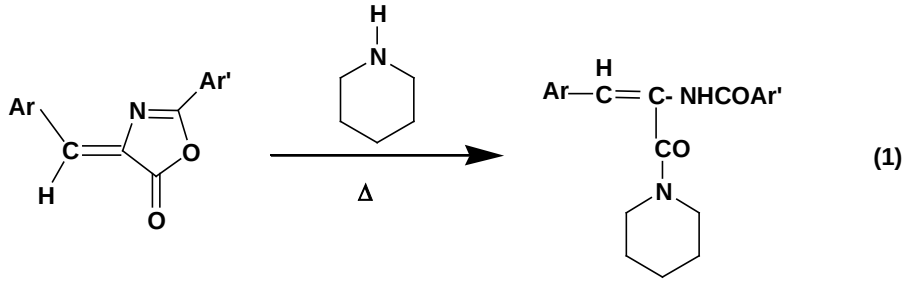


Z-1$_{a-e}$

Fig. (1)

Configuration assignment and structure proof of benzamides $\underline{3}_{a-e}$

The treatment of (Z)-4-(5-sustituted furylidene)-2- aryloxazolin -5-ones$\underline{1}_{a-e}$ with piperidine in acetonitrile gave mainly the corresponding 4-Substituted-N-[2-(5-substituted-furan-2-yl)-1-(piperidine-1-carbonyl)-vinyl]-benzamide, as indicated from the elemental analysis, UV, IR and NMR, equation (1), (see Experimental part).



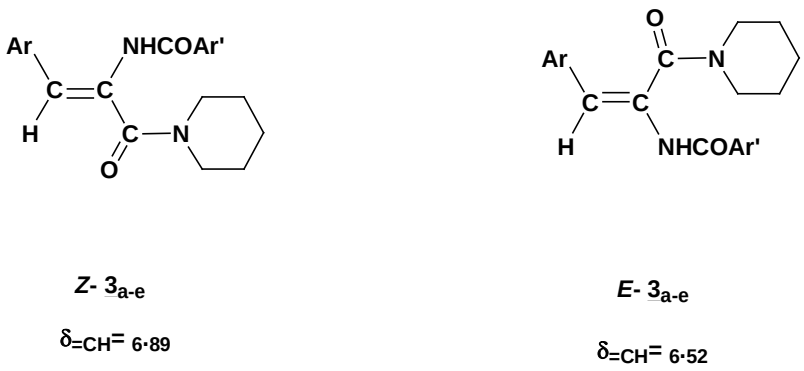
(1)

***Z*-$\underline{1}_{a-e}$** **$\underline{3}_{a-e}$**

The elemental analysis, UV, IR and NMR indicates the aminolysis ring opening and the mechanism proceeds by nucleophilic acyl substitution reaction. The NMR indicates the formation of exclusively one isomer as shown from the single vinylic proton at C_3 which resonating at δ (6.93-7.09) ppm. The C_2 ethylenic ^{13}C-NMR chemical shift for $\underline{3}_a$ (128.45ppm) resemble those reported for ethyl-α-cyanocinnamates, α-cyano cinnamides, ethyl (α-ethoxycarbonyl) cinnamates[45-46], methyl acrylate and acrylic acid[47]. On the other hand, the chemical shifts of olefinic carbon C_3 showed resonance signals at 148.26 ppm for $\underline{3}_a$ which is less than reported for benzylidene malononitrile[48] and methyl acrylate[49], but agree with the calculated values. Carbonyl carbon C_1 chemical shifts appear at δ 173.28 ppm for $\underline{3}_a$. All these values agree with the calculated values using chem. draw program.

Though compounds $\underline{3}_{a-e}$ can exist as E- or Z-configurational isomers, actually only one form of these isomers was exclusively obtained. This makes the assignment difficult due to the absence of comparison between the two configurational isomers. The more stable form whether the benzamido or piperidino group should be trans to the aryl group can not be decided on steric grounds, this is because in either cases there are a bulky groups in the cis position that gave rise to considerable non-bonding interactions The configuration assignments of $\underline{3}_{a-e}$ compounds were based on NMR analysis. The calculated chemical shifts of vinylic protons for Z- and E- steroisomers by applying the ^{1}H-NMR additivy increment rules[50-52] and the gated decoupling technique[53-54], gave conclusive information concerning the relative configuration of C and H in trisubstituted alkenes[50.53].The calculated chemical shifts of the vinylic protons for $\underline{3}_{a-e}$ are 6.89 ppm for the Z-configuration and 6.52 ppm for E-configuration. These values were in agreement with the Z- configuration for compounds $\underline{3}_{a-e}$ because their vinylic proton is actually resonating at δ (6.93-7.09) ppm, (see Experimental part).

The relatively higher chemical shift of the vinylic proton of Z-isomer than that of the E- one could be attributed to the higher shielding effect of the amido group and/or "anisotropic effect" which lie in the same side of double bond with the vinylic proton of the E-isomer[55]. Furthermore, a more effective factor is the conjugation of olefinic bond and carbonyl group can be assumed to lead to an increase of the positive charge on C_β in the E-isomer, Fig.(2).



***Z*- 3_{a-e}**

$\delta_{=CH}$= 6·89

***E*- 3_{a-e}**

$\delta_{=CH}$= 6·52

Fig. (2)

Also, the relative configuration of double bond in compounds 3_{a-e} can be confirmed from $^{3}J_{CH}$ of the carbonyl carbon at C_1 of ^{13}C signal at 173.28 ppm in the coupled ^{13}C-NMR spectrum. As a result of this coupling, a triplet at 173.28 ppm (J =11.25 Hz) for 3_a (R= H) was observed.

The $^{3}J_{CH}$ value = (9-11) Hz coupling points to a cis-configuration[53] of carbonyl carbon (C_1) and olefinic (H_3). Consequently, the benzamido and aryl groups are located in cis-position; and compound 3_a has the Z- configuration. Similarly compounds 3_{b-e} exists in the Z-configuration.

Kinetic studies for the reaction of 1_{a-e} with piperidine in acetonitrile

Although unsaturated oxazolinones well known, there have been very few reported studies on the quantitative aspects of their reactivity. The reactions of oxazolinone are usually considered to be a typical example of ester reactions. However, Olson and co-workers[54-55] have been reported that the ring opening reactions of these types of esters in basic and strongly acidic solutions resulted in the expected acyl-oxygen fission (a), while in the neutral or slightly acidic solutions alkyl-oxygen bond fission (b) is the predominating pathway, Fig. (4)

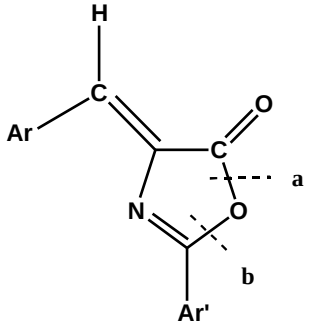


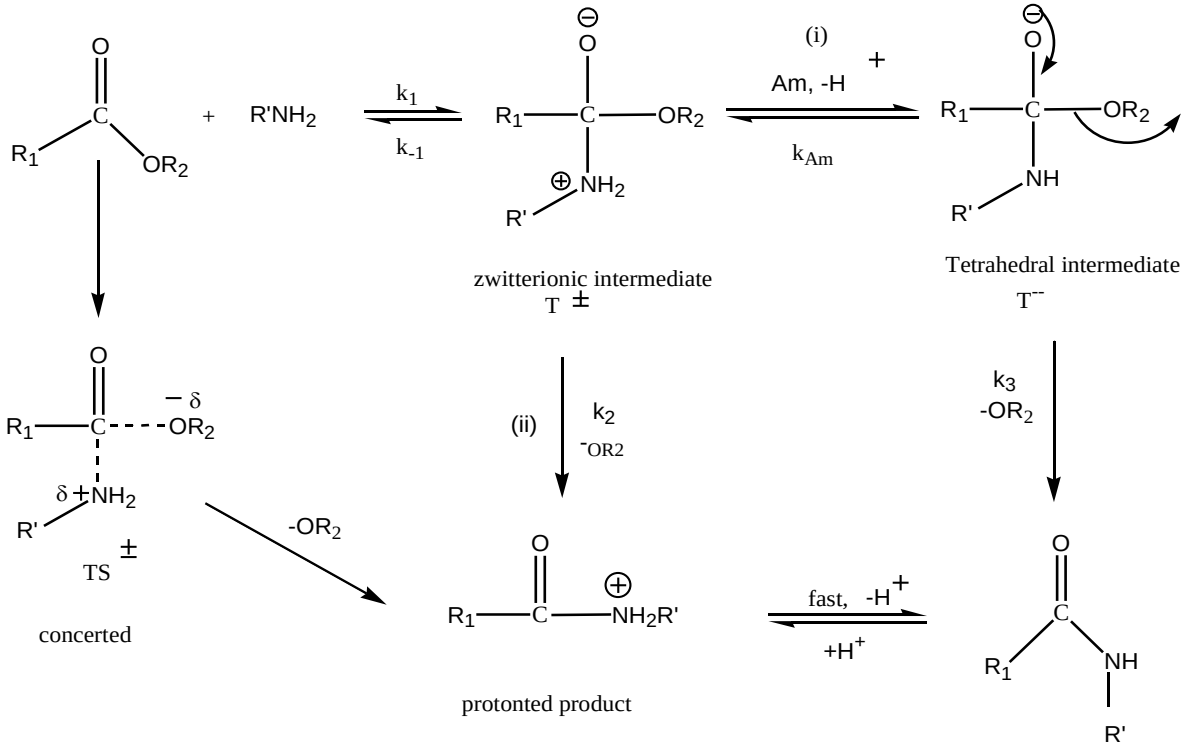
Fig. (4)

Kinetic studies and mechanism for the reaction of 1_{a-e} with piperidine in acetonitrile

Castro and coworkers[56-58] have been reported a number of mechanistic studies on the aminolysis of esters. These studies showed that most aminolysis of esters proceed by a stepwise mechanism through a zwitterionic tetrahedral intermediate $T^{\pm}$, or concertedly transition state $TS^{\pm}$, depending on the amine, substrate and solvent involved.

Shawali etal[59] proposed a stepwise mechanism with rate limiting break down of a tetrahedral intermediate $T^{\pm}$ for the reaction of an ester with amine in dioxane. Their kinetic results were compatible with the stepwise mechanism involving two reaction pathways , one overall third–order , k_3, process pathway (a). Alternative pathway (b) is second-order, k_2, and proceeds through a concerted mechanism involving a concerted transition state $TS^{\pm}$), Scheme

(2). Linear free energy relationships (LFERS) have been employed as one of the most popular probes for the determination of the reaction mechanism.



Scheme (2)

In this work we are interested to study the substituent effect of para and 5- substituents in aromatic rings of both non leaving (Ar) and leaving (Ar') moieties on the reactivity of oxazolinone towards piperidine. The rate constants of the reactions of substituted oxazolinones $\underline{1}_{a\text{-}e}$ with piperidine in acetonitrile at 25, 30, 35, 40, 45 and 50^0C were determined, Table (1). The kinetic runs were measured spectrophotometrically where piperidine concentration was in large excess. Under these conditions of pseudo first-order kinetics, rate constants $k_{obs.}$ (sec^{-1}) were obtained. Plots of $k_{obs.}$ (sec^{-1}) versus piperidine concentrations gave straight lines passing through the origin with slopes equal to the second-order rate constants (k_A), indicating that the reaction is not catalyzed by piperidine and the reaction obeys a clean second–order rate law. It is clear from the kinetics data that the electronic effects exert a moderate influence on the reactivity of reaction, Table (1).

The reaction of (z)-4-(substituted furylidene)-2-(4-substitutedphenyl)oxazolin-5-ones$\underline{1}_{a\text{-}e}$ .with piperidine depends on the nature of aromatic ring (Ar) of the arylidene moiety which playing an important role in the reactivity of oxazolinone.

The reactivity of (z)-4-(5-chlorofurylidene)-2-phenyl oxazolin-5-ones $\underline{1}_c$ with piperidine is (4 to 6) times faster than that for (z)-4-(5-methyfurylidene)-2-phenyl oxazolin-5-one $\underline{1}_b$. This increasing in the reactivity by introducing electron withdrawing group in aryl ring may be attributed to increase the electrophilicity of carbonyl carbon of oxazolinone in ground state beside it stabilizes the formed negative charge on oxygen atom of activated complex, while electron donating groups have opposite effect.

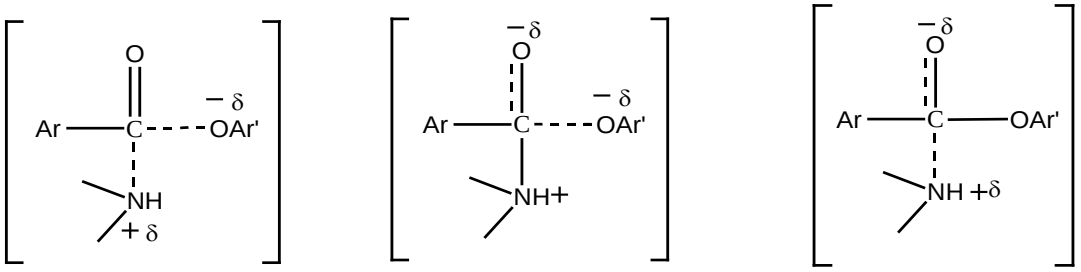
The aminolysis rates of substituted oxazolinone decrease according to the following order:

5-Cl furyl > 5-H furyl≈ p'-Me phenyl ≈ p'-Cl phenyl > 5-Me furyl .

It is customary to correlate the effect of 5-substituents in the furyl ring with the σ-Hammett constants. Plots of log k_A for these reactions versus σ-Hammett values for compounds $1_{a\text{-}c}$ gave good straight lines at different temperatures with slope (ρ) ranging from + (1.46 - 1.79), In this work, we invoke the mechanistic criteria for the studied reaction based

on the sign of reaction constant ρ in the substrates $\underline{1}_{a\text{-}c}$. The estimated ρ values for the reactions of piperidine with oxazolinones are exceptionally moderate and the formed activated complex has an anionic character[60].

Three transition states for acyl-oxygen fission can be proposed to account for the present result: 1) TS_1 represents the transition-state structure for the reaction in which the nucleophilic attack and departure of the leaving group occur simultaneously (a concerted mechanism). 2) TS_2 represents the transition-state structure for the stepwise mechanism in which leaving group departure occurs at rate-determining step. 3) TS_3 the transition-state structure for the stepwise mechanism in which leaving group departure occurs in fast step, Fig. (5).



TS_1 TS_2 TS_3

Table (1): Rate constants and activation parameters for the reaction of oxazolinones $\underline{1}_{a\text{-}e}$ with piperidine in acetonitrile

			$10^2 x K_A$ l $mol^{-1} sec^{-1}$								
Cpd	X	y	25^0C	30^0C	35^0C	40^0C	45^0C	50^0C	E_a Kcal mol^{-1}	$\Delta H^{\#}$ Kcal mol^{-1}	$-\Delta S^{\#}$ Kcal mol^{-1}
1_a	H	H	5.21	8.42	10.62	11.31	12.13	13.80	6.69	6.09	43.93
1_b	CH_3	H	2.51	4.31	5.42	6.02	6.59	7.11	7.31	6.71	42.25
1c	Cl	H	13.37	20.03	23.83	25.24	26.93	28.43	5.10	4.51	47.33
	ρ		+1.79	+1.63	+1.57	+1.42	+1.49	+1.46			
1_d	H	CH_3	5.71	8.61	11.01	11.51	12.31	14.00	6.21	5.61	45.35
1_e	H	Cl	5.19	7.94	10.92	11.25	12.11	13.71	6.83	6.23	43.45

The aminolysis of oxazolinones $\underline{1}_{d\text{-}e}$ which contain (4-Cl and 4-CH_3) in the phenyl ring (Ar') of leaving group showed a slight difference in rate constant compared to unsubstituted one 1_a. This slight change in the reaction rate ruled out the concerted mechanism (TS_1) and indicated that the expulsion of the leaving group did not effect by changing the substituent (fast step). So the expulsion of the leaving group is not the rate determining step for postulated stepwise mechanism. The small ρ values for the substituents on the non-leaving groups can explain as follow on the basis of the introduction of the electron withdrawing substituents will stabilize the formed negative charge on oxygen atoms while it destabilizes

the positive charge on nitrogen atom of piperdonium moiety in transition state, thus the net value of reaction constant ρ must equal algebraic summation of the two created opposite charges in preformed transition state (compensated value of ρ value).Therefore, the linear free energy correlation for such reaction can be written as follow.

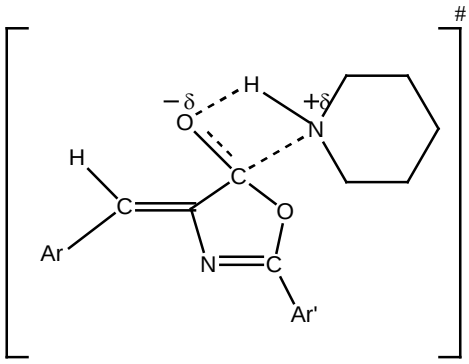
$$\log\frac{k_{P-X}}{k_{P-H}} = (+ve)\rho_O\sigma + (-ve)\rho_N\sigma = ((+ve)\rho_O + (-ve)\rho_N)\sigma$$

$$\because (+ve)\rho_O \rangle (-ve)\rho_N$$

$$\therefore \log\frac{k_{P-X}}{k_{P-H}} = (\Delta + ve)\rho\sigma$$

The temperature dependence of ρ for the reaction under investigation which fit to the ρσ relationship does not deteriorate as the temperature is changed. Since the nucleophilic attack of piperidine on carbonyl of oxazolinone obeyed Hammett equation, thus: $\rho\sigma = \pm\delta_X \Delta H/2.303RT$ and in agreement with the decrease of ρ with increasing the temperature as shown in Table (1).

The thermodynamic parameters of activation and rate data at sex different temperatures are summarized in Table (1). The entropy ($\Delta S^{\#}$) and the enthalpy ($\Delta H^{\#}$) values indicated that these reactions are almost isoentropic and the difference in reactivity is enthalpy dependent (enthalpic control reaction). The negative $\Delta S^{\#}$ values are as expected for bimolecular nucleophilic substitution reaction and explained on the concept of the transition state involves much greater charge separation than that existing in the reactants. Therefore, the change from reactants to the more polar transition state will be accompanied by a considerable loss of solvent freedom causing a consequent decrease in entropy. It was observed that compounds containing electron withdrawing substituents showed more negative $\Delta S^{\#}$ values than that of electron donating substituents. This is presumably explained on the fact that the extent of the bond formation in case electron withdrawing substituents are greater than that of electron donating one in the corresponding activated complex. Further, the formation of rigid cyclic H-bonding transition state reflects the high entropy values in contact to that postulated a stepwise mechanism in which the formation of tetrahedral intermediate is the rate-determining step. Therefore, the large negative $\Delta S^{\#}$ values are acceptable for the formation of the hydrogen bonded, four member cyclic ($TS^{\pm}$) [61], Fig. (6).



$TS^{\#}$

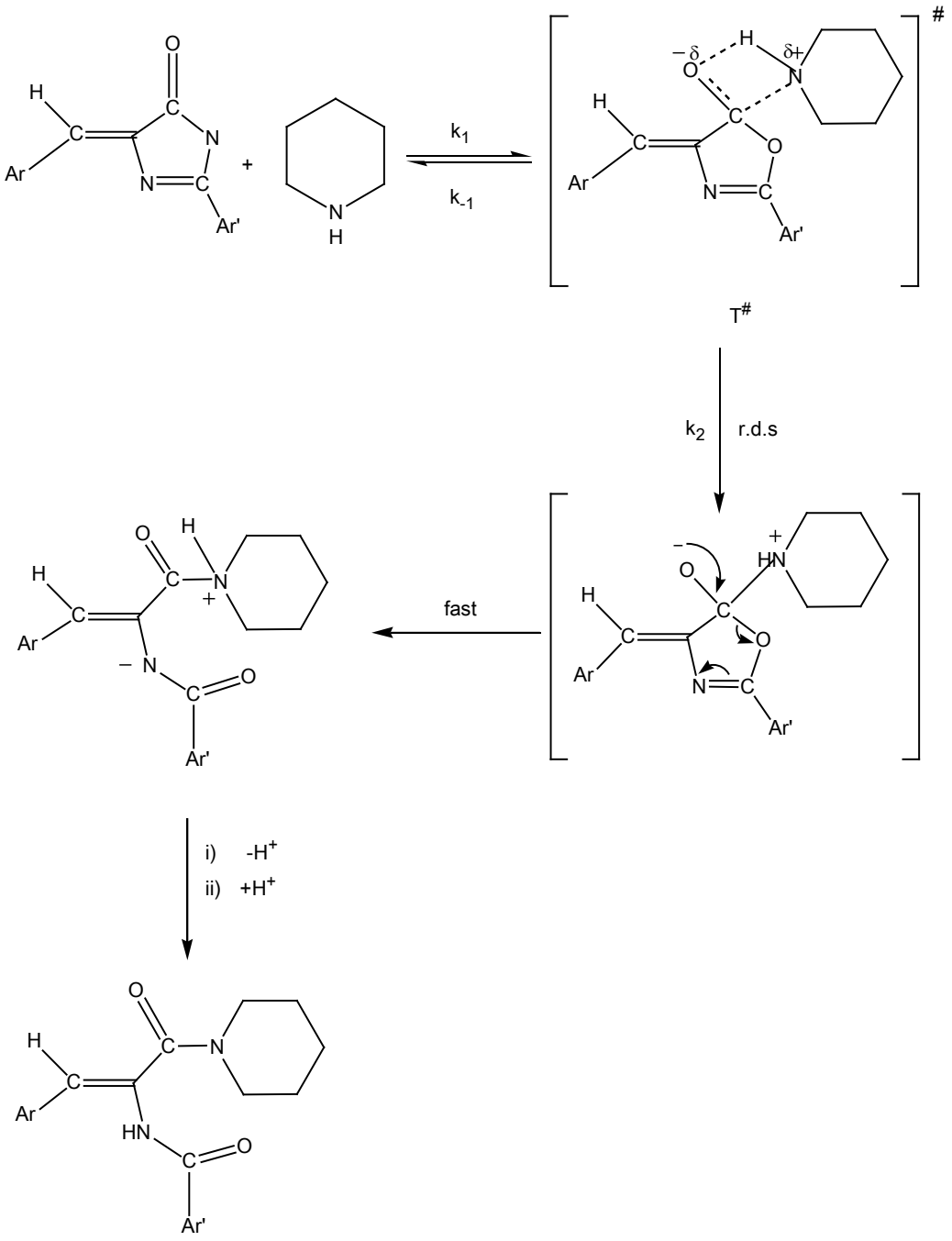
Fig. (6)

The relatively small $\Delta H^{\#}$ values with large negative $\Delta S^{\#}$ values are consistent with the proposed transition state structure $(TS^{\pm})$. The small $\Delta H^{\#}$ values are due to a large energy gain in C-N bond formation with respect to energy loss in C=O bond cleavage in addition the assistance in the polarization of C=O by the hydrogen bonding.

A linear free energy relationship maintaining its linear form at more than one temperatures implies a constraint on enthalpies and entropies, thus for such studied reaction which showed correlation at more than one temperatures would be obey the following isokinetic, equation (4).

$$\Delta H^{\#} = \beta \Delta S^{\#} \qquad (4)$$

Plot $\Delta H^{\#}$ versus $\Delta S^{\#}$ showed a reasonable straight line with a slope for isokinetic temperature β which found to be equal 434 K^0(r = 0.99), 464 K^0(r = 0.97) for the reactions of substitutedfuryl $\underline{1}_{a\text{-}c}$ with piperidine respectively. These isokinetic temperatures are far from those employed in the kinetic runs $(25\text{-}50)^0$C. The linear plots of log k_A at different temperatures against $\Delta H^{\#}$ and $T\Delta S^{\#}$ (not shown) beside plots of log k_A at certain temperature against log k_A at another temperature (not shown) and isokinetic plots of $\Delta H^{\#}$ versus $\Delta S^{\#}$ indicated that the reaction series followed the same mechanism. The main factor governed the nucleophilic ring opening of oxazolinone is the activation enthalpy $\Delta H^{\#}$ which tends to be decreased with increasing in substrate reactivity. The estimated positive ρ values, thermodynamic parameters and reaction rate constants for both reactions with piperidine are consisting with stepwise mechanism, where the first stage is a slow perpendicular nucleophilic attack of piperidine on carbonyl carbon forming the intermediate ($T^{\#}$) passing through a cyclic zwitterionic transition state followed by expelling of the leaving group. Finally deprotonation of piperdonium moiety is followed by protonation of benzamido nitrogen afforded the final product, Scheme (3).



Ar = furyl, 5-CH_3furyl , 5-Clfuryl, C_6H_5, 4-$CH_3C_6H_4$, 4-ClC_6H_4, 4-BrC_6H_4, 4-CH_3O C_6H_4 , 4-O_2N C_6H_4.

Ar'= C_6H_5, 4-CH_3 C_6H_4, 4-Cl C_6H_4.

Scheme (3).

Applying steady state conditions to the intermediate [$T^{\#}$]:-

$$\frac{d[T^{\#}]}{dt} = 0$$

$$k_1[Oxa][Hyd] - k_{-1}[T^{\#}] - k_2[T^{\#}] = 0$$

$$[T^{\#}] = \frac{k_1[Oxa][Hyd]}{k_{-1} + k_2}$$

since $\frac{d[prod]}{dt} = k_2[T^{\#}]$

$$\frac{d[prod]}{dt} = \frac{k_1 k_2[Oxa][Hyd]}{k_{-1} + k_2}$$

where $k_2 >> k\text{-}1$

$$\frac{d[prod]}{dt} = \frac{k_1 k_2[Oxa][Hyd]}{k_2}$$

$$\frac{d[prod]}{dt} = k_1[Oxa][Hyd]$$

where k_1. is the observed rate constant

Experimental section

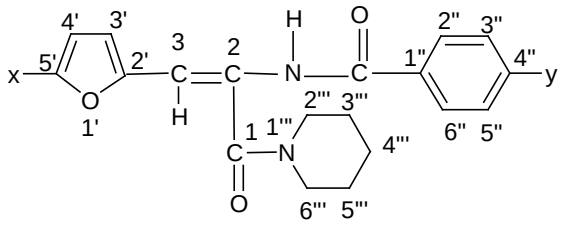
Piperidine and acetonitrile used are BDH.

a) Synthesis of (Z)-4-(substitutedfurylidene)-2-aryloxazolin-5-ones $\underline{1}_{a\text{-}e}$

(Z)-4-(substitutedfurylidene)-2-aryloxazolin-5-ones were prepared and purified as previously reported[1-5].

b) Reaction of substituted oxazolinones $\underline{1}_{a\text{-}e}$ with piperidine **in acetonitrile**

General procedure: A (0.01mole) of piperidine was added to a solution of $\underline{1}_{a\text{-}e}$ (0.005mole) in acetonitrile (15 ml). The reaction mixture was refluxed for two hours. The reaction mixture was cooled and poured into cold water. The separated solid was filtrated and crystallized from ethanol to give the corresponding 4-Substituted-N-[2-(5-substituted-furan-2-yl)-1-(piperidine-1-carbonyl)-vinyl]-benzamides $\underline{3}_{a\text{-}e}$.



$\underline{3}_{a\text{-}e}$

N-[2-(furan-2-yl)-1-(piperidine-1-carbonyl)-vinyl] benzamide 3_a: Yield (80 wt %), m.p. (153-155^{0}C). UV (acetonitrile): $\lambda_{max.}$ nm = 302 and 226, ε = 12397, 10315. IR (KBr) ν cm^{-1}: 1597 (conjugated C=C), 1656 (C=O amide), 1675 and (C=O piperidino). ^{1}H-NMR (DMSO-d_6) δ ppm: 9.43 ppm (1H, s, NH amide), 8.12 (2H, d, $H_{2",6"}$), (1H, d, $H_{5'}$), 7.62 ppm (1H, t, $H_{4"}$), 7.42 (2H, t, $H_{3",5"}$), 6.93 (1H,s, H_3 vinylic), 6.58 (1H, d, $H_{3'}$), 2.88 ppm (4H,t, $H_{2'}$", $_{6"}$) and 2.05 ppm (6H,m, $H_{3'}$", $_{4"}$', $_{5"}$). ^{13}C-NMR (DMSO-d_6) δ ppm: 173.28 (C=O piperidino), 167.10 (C=O amide), 134.67 (C_2), 128.45 (C_3), 148.26, 122.53, 133.80, 134.48,

125.94 ,111.48 (aromatic carbons) and 56.23, 41.57, 39.22 (piperidine carbons). Calcd. for $C_{19}H_{20}N_2O_3$: C ,70.37; H,6.17; N, 8.64, found : C , 70.43; H,6.11; N, 8.54.

N-[2-(5-methylfuran-2-yl)-1-(piperidine-1-carbonyl)-vinyl] benzamide $\underline{3}_b$: Yield (74 wt %), m.p. (158-160^{0}C). UV (acetonitrile): λ_{max}. nm = 318 and 226, ε = 14423, 11006. IR KBr) ν cm^{-1}: 1589 (conjugated C=C), 1662 (C=O amide) and 1673 (C=O piperidino) . ^{1}H-NMR (DMSO-d_6) δ ppm: 9.22 (1H, s, NH amide), 7.88 (2H, d, $H_{2",6"}$), 7.36 (3H, m, $H_{3",4",5"}$), 7.09 (1H, s, H_3 vinylic), 6.73 (1H, d, $H_{3'}$), 6.66 (1H, d, $H_{4'}$), 2.73 ppm (4H,t, $H_{2",\ 6"}$), 2.11 (3H, s, CH_3), and 1.89 ppm (6H,m, $H_{3",\ 4",\ 5"}$) . Calcd.for $C_{20}H_{22}N_2O_3$: C, 71.01; H, 6.51; N, 8.28, found : C, 71.23; H, 6.46; N,8.19.

N-[2-(5-chlorofuran-2-yl)-1-(piperidine-1-carbonyl)-vinyl] benzamide $\underline{3}_c$: Yield (84 wt %), m.p. (168-170^{0}C). UV (acetonitrile): λ_{max}. nm = 304 and 227, ε = 14235, 11916. IR KBr) ν cm^{-1}: 1602 (conjugated C=C), 1667 (C=O amide) and 1687 (C=O piperidino). ^{1}H-NMR (DMSO-d_6) δ ppm: 8.96 (1H, s, NH amide), 7.79 (2H, d, $H_{2",6"}$), 7.32 (3H, m, $H_{3",4",5"}$), 7.03 (1H, s, H_3 vinylic), 6.33 (1H, d, $H_{3'}$), 6.13 (1H, d, $H_{4'}$), 2.93 ppm (4H,t, $H_{2",\ 6"}$) and 1.75 ppm (6H,m, $H_{3",\ 4",\ 5"}$). Calcd.for $C_{19}H_{19}N_2O_3Cl$: C, 63.60; H,5.30; N,7.81 found : C, 63.52; H,5.35; N,7.85.

4-Methyl N-[2-(furan-2-yl)-1-(piperidine-1-carbonyl)-vinyl]- benzamide 3_d: Yield (76 wt %), m.p. (159-161^{0}C). UV (acetonitrile): λ_{max}. nm =272 and 224, ε = 20225, 21000. IR (KBr) ν cm^{-1}: 1598 (conjugated C=C), 1672 (C=O amide) and1677 (C=O piperidino). ^{1}H-NMR (DMSO-d_6) δ ppm: 9.37 (1H, s, NH amide), 7.86 (2H, d, $H_{2",6"}$), triplet at δ 7.47 ppm (2H, t, $H_{3",5"}$), 7.32 (1H, t, $H_{5'}$)), 7.25 (1H, t, $H_{3'}$),), 7.19 (1H, t, $H_{4'}$), 7.06 (1H, s, H_3 vinylic), 2.93 ppm (4H,t, $H_{2",\ 6"}$), 2.43 (3H, s, CH_3), and 1.94 ppm (6H,m, $H_{3",\ 4",\ 5"}$). Calcd.for $C_{20}H_{22}N_2O_3$: C, 71.01; H, 6.51; N, 8.28, found : C, 71.09; H, 6.66; N,8.31.

4-Chloro N-[2-(furan-2-yl)-1-(piperidine-1-carbonyl)-vinyl]- benzamide 3_e:Yield (81 wt %), m.p. (167-169^{0}C). UV (acetonitrile): λ_{max}. nm =282 and 223, ε = 20105, 20755. IR (KBr) ν cm^{-1}: 1605 (conjugated C=C), 1662 (C=O amide) and1675 (C=O piperidino). ^{1}H-NMR (DMSO-d_6)) δ ppm: 9.63 (1H, s, NH amide), 7.96 (2H, d, $H_{2",6"}$), 7.53 (2H, d, H $H_{3",5"}$)), 7.46 (4H, m, $H_{2',3',4',5'}$), 7.02 (1H, s, H_3 vinylic), 3.09 ppm (4H,t, $H_{2",\ 6"}$) and 2,03 ppm (6H,m, $H_{3",\ 4",\ 5"}$). Calcd.for $C_{19}H_{19}N_2O_3Cl$: C, 63.60; H,5.30; N,7.81 found : C, 63.73; H,5.26; N,7.93.

Kinetic measurements

Kinetics of the reaction of oxazolinone derivatives with hydrazine in acetonitrile

The reaction of (Z)-4-(substitutedarylidene)-2-aryloxazolin-5-ones $\underline{1}_{a-e}$ with piperidine in acetonitrile to form the corresponding 4-Substituted-N-[2-(5-substituted-furan-2-yl)-1-(piperidine-1-carbonyl)-vinyl]-benzamides $\underline{3}_{a-e}$, were followed spectrophotometrically at 25, 30, 35, 40, 45 and 50^{0}C using Jasco(V-350UV-VIS) spectrophotometer. The solutions of oxazolinones and piperidine were separately allowed to attain the desired temperature ± 0.5^{0}C in a thermostated bath before being mixed. Measurements were usually carried by following the decrease of the oxazolinones absorbance with time at wavelength (λ) = 385±5 nm. The reactions were performed under pseudo first-order conditions where the piperidine concentration was excess compared to that of substrate, [(100:1) to (350:1)]. The first-order rate constants (k_ψ) were calculated by the least squares method from the linear plots of ln (A_t-A_∞) versus time (t). Plots of k_ψ versus piperidine concentrations gave straight lines passing through the origin with slopes equal to second-order rate constants (k_A).

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